The Andrulis Patent concerns only thalidomide and pentoxyifylline; it does not disclose using any of the specific TNF antagonists claimed in the present application.

Thalidomide and pentoxyifylline are not pure TNF antagonists, as are the pharmaceutical compounds of the present invention. For example, as mentioned in the Andrulis patent, thalidomide also inhibits IL-1 beta and bFGF. Additionally, thalidomide has known antiagiogenic activity, which pure TNF antagonists do not have.

Pentoxifylline, like thalidomide, is not a pure TNF antagonist, as are all of the biopharmaceuticals claimed in the present patent application. Pentoxifylline has significantly different biochemical and pharmacologic properties from the pure TNF antagonists which are in the claims of this application.

Pentoxifylline is a tri-substituted xanthine derivative designated chemically as 1-(5-oxohexyl)-3, 7-dimethylxanthine. It is neither an anti-TNF monoclonal antibody nor an agent containing soluble TNF receptors, as are the therapeutic agents in the claims of this application.

The following is a description of the mode of actionof pentoxifylline in the Andrulis Patent:

"Pentoxifylline and its metabolites improve the flow properties of blood by decreasing its viscosity. In patients with chronic peripheral arterial disease, this increases blood flow to the affected microcirculation and enhances tissue oxygenation. The precise mode of action of pentoxifylline and the sequence of events leading to clinical improvement are still

to be defined. Pentoxifylline administration has been shown to produce dose-related hemmotheologic effects, lowering blood viscosity, and improving erythrocyte flexibility. Leukocyte properties of hemorrheologic importance have been modified in animal and in vitro human studies. Pentoxifylline has been shown to increase leukocyte deformability and to inhibit neutrophil adhesion and activation. Tissue oxygen levels have been shown to be significantly increased by therapeutic doses of pentoxifylline in patients with peripheral arterial disease. "Lastly, the Andrulis patent only concerns HIV infection.

The Alexander Patent concerns only chronic pelvic pain syndrome, which includes chronic prostatitis. There is a disclosure of TNF antagonists, including etanercept, as therapeutic agents for certain diseases; such as the treatment of arthritis. However, arthritis is not related to viral diseases, or neurological disorders, so it is not obvious that these agents would be useful for the treatment of viral diseases or neurological disorders. Indeed, there is no disclosure in Alexander regarding the use of TNF antagonists to treat viral conditions and it is not obvious to do so.

The Christensen patent discloses the use of compounds of a certain formula ("Formula 1") to inhibit the production of TNF. This patent is not applicable to the present application for two reasons:

1. The pharmaceutical compounds claimed in the present application are not of the form of Formula 1 as discussed in the Christensen patent; and

2. The pharmaceutical compounds claimed in the present application are not compounds which inhibit the production of TNF; rather these compounds interfere with the action of TNF, but have no direct effect on the production of TNF. Compounds which interfere with the production of TNF are in a completely different class from the medications claimed in the present application.

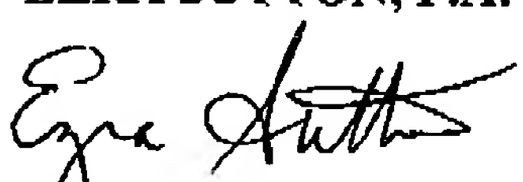
Thus, the Christensen patent is concerned with compounds of a completely different structure and class than the biopharmaceutical compounds claimed in the present application.

For these reasons, Claims 1 to 84 of the present application are patentable over these patents, and are not obvious in view of these patents.

The Examiner has rejected Claims 1 to 84 based on double patenting using U.S. Patent No. 6,177,077 and U.S. Patent No. 6,015,557. These rejections are overcome by filing the enclosed two (2) terminal disclaimers with respect to these patents.

This application is in condition for allowance, and such action is respectfully requested.

Respectfully submitted,
EZRA SUTTON, P.A.



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